

**REMARKS**

**I. Status of the Claims**

Claims 17-28, 30-31, and 33-35 are pending in this application. Claim 31 has been amended. Claim 32 has been canceled. No new matter has been added by this Amendment.

Applicants thank the Examiner for consideration of this application during the May 6, 2003, in-person interview. The Examiner has withdrawn the 35 U.S.C. §112, second paragraph, rejections. Claims 28, 30, and 31 have been allowed.

**II. Rejections Under 35 U.S.C. § 112, First Paragraph**

The Examiner has rejected claims 17-27 and 32-35 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. Applicants respectfully request reconsideration of these claims in light of the reasons already of record and the additional data provided below. Applicants provide the data below, which gives examples of the activity of the claimed group A streptogramin derivatives, alone and in combination with group B streptogramin derivatives, such as pristinamycin IB (PIB), pristinamycin IA (PIA), or quinupristin (Q). As acknowledged in the May 2003 Interview Summary, Applicants appreciate the Examiner's after-final consideration of this data.

The compounds identified as Example Nos. 1-23 provided in the chart below correspond with the compounds identified in the preparatory Example Nos. 1-23 set forth in the specification. An outline of the testing protocol is provided below the chart.

example N°	<i>In vitro</i> activity  <i>S.aureus</i> IP8203  MIC (mg/l) Alone	<i>In vitro</i> activity <i>S.aureus</i> IP8203  MIC (mg/l)  Combined with PIB	<i>In vivo</i> activity  <i>S.aureus</i> IP8203  Curative Dose 50 (mg/kg)	
			Combined with Q or PIB*	Combined with PIB or PIA*
			s.c.	p.o.
1	>32	8	>150*	75*
2	32	4	36*	80
3	>128	2	65	>150
4	128	1	75	110
5	64	4	40*	>150
6	>128	2	40	110
7	>128	4	50*	>150*
	4	2	28*	>150
8	>128	2	34*	>150*
	16	2	32	>150
9	128	8	110	>150
10	64	1	32	100
11	128	1	75	110
12	16	0.5	32	100
13	128	4	Nd	Nd
14	4	1	15	120
15	64	0.5	36	150
			13*	
16	>128	4	130	>150

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example N°	<i>In vitro</i> activity  <i>S.aureus</i> IP8203  MIC (mg/l) Alone	<i>In vitro</i> activity <i>S.aureus</i> IP8203  MIC (mg/l)  Combined with PIB	<i>In vivo</i> activity  <i>S.aureus</i> IP8203  Curative Dose 50 (mg/kg)	
			Combined with Q or PIB*	Combined with PIB or PIA*
			s.c.	p.o.
17	32	1	32	36
18	8	0.5	36*	42
19	4	1	32*	32
20	32	4	50*	100
21	16	0.5	24*	24
22	64	2	42*	120
23	nd	nd	<30	>100

### **In vitro bacteriostatic activity**

The bacteriostatic activity of the compounds was determined according to the U.S. standards (Antimicrobial Susceptibility Testing: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically. 1992 National committee for clinical Laboratory Standards, M7-A2, Villanova, PA.).

Two-fold dilutions of the 1280 mg/l antibacterial stock solution tested were added to molten Mueller-Hinton agar supplemented with 25 mg/l Mg++ and 50 mg/l CA++ (1 part of antibacterial solution for 9 parts of liquid agar), then poured into plates. A multipoint inoculator was used to apply spots of about  $10^4$  colony forming units (cfu) of each strain tested onto agar. After inoculation plates were incubated 18 hours at 37°C.

The minimum inhibitory concentration (MIC) was defined as the lowest concentration (mg/l) which completely inhibited the growth of bacteria.

**In vivo antibacterial activity in the model of *staphylococcus aureus* mouse septicemia**

Mice (6 to 8 per group) were inoculated intraperitoneally with 0.5 ml of the bacterial strain cultured under shaking in Brain Heart Infusion AT 37°C and diluted in 7.5% porcine mucine so as to obtain about 10<sup>6</sup> cfu/ml. Under these conditions, infected untreated controls die in 24 to 48 hours.

The compound tested was administered by the s.c. (subcutaneous) or the oral routes twice on the day of inoculation, the first dose being given 1 hour after infection and the second dose 2 hours after infection.

The vehicle was an aqueous solution or a suspension in 0.9% NaCl aqueous solution added with 0.1% polysorbate 80 (Prolabo). The administered volume was 1 ml/mouse per treatment.

Three to 6 doses up to 150 mg/kg were used.

The Curative Dose 50 (mg/kg), calculated 7 days post infection, was defined as the dose which protected 50% of the infected treated mice when all the infected untreated controls died.

Accordingly, Applicants respectfully request withdrawal of the § 112, first paragraph, rejection over claims 17-27 and 32-35.

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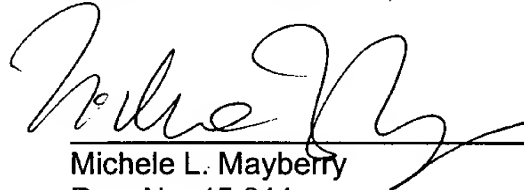
III. **Conclusion**

In view of the foregoing Amendment and Remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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